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Superior Exercise Performance in Lifelong Tibetan Residents of 4,400 m Compared With Tibetan Residents of 3,658 m

LINDA S. CURRAN,[1]* JIANGUO ZHUANG,[2]
TARSHI DROMA,[2] AND LORNA G. MOORE[1,3]
[1]*Department of Anthropology, University of Colorado at Denver, Denver, Colorado 80217-3364*
[2]*Tibet Institute of Medical Sciences, Lhasa, Tibet Autonomous Region, China 850000*
[3]*Cardiovascular Pulmonary Research Laboratory, University of Colorado Health Sciences Center, Denver, Colorado 80262*

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ABSTRACT Few environments challenge human populations more than high altitude, since the accompanying low oxygen pressures (hypoxia) are pervasive and impervious to cultural modification. Work capacity is an important factor in a population's ability to thrive in such an environment. The performance of work or exercise is a measure of the integrated functioning of the O_2 transport system, with maximal O_2 uptake ($\dot{V}O_{2max}$) a convenient index of that function. Hypoxia limits the ability to transport oxygen: maximal O_2 uptake decreases with ascent to high altitude, and years of high altitude residence do not restore sea level $\dot{V}O_{2max}$ values. Since Tibetans live and work at some of the highest altitudes in the world, their ability to exercise at very high altitude (>4,000 m) may define the limits of human adaptation to hypoxia. We transported 20 Tibetan lifelong residents of ≥4,400 m down to 3,658 m in order to compare them with 16 previously studied Tibetan residents of Lhasa (3,658 m). The two groups of Tibetans were matched for age, weight, and height. All studies were performed in Lhasa within 3 days of the 4,400 m Tibetans' arrival. Standard test protocol and criteria were used for attaining $\dot{V}O_{2max}$ on a Monark bicycle ergometer, while measuring oxygen uptake ($\dot{V}O_2$, ml/kg − min STPD), heart rate (bpm), minute ventilation ($\dot{V}_E$, 1/min BTPS), and arterial oxygen saturation (Sa_{O_2}, %). The 4,400 m compared with 3,658 m residents had, at maximal effort, similar $\dot{V}O_2$ (48.5 ± 1.2 vs. 51.2 ± 1.4 ml/kg − min, P = NS), higher workload attained (211 ± 6 vs. 177 ± 7 watts, $P < 0.01$), lower heart rate (176 ± 2 vs. 191 ± 2 bpm, $P < 0.01$), lower ventilation (127 ± 5 vs. 149 ± 5 l/min BTPS, $P < 0.01$), and similar Sa_{O_2}(81.9 ± 1.0 vs. 83.7 ± 1.2%, P = NS). Furthermore, over the range of submaximal workloads, 4,400 m compared with 3,658 m Tibetans had lower $\dot{V}O_2$ ($P < 0.01$), lower heart rates ($P < 0.01$), and lower ventilation ($P < 0.01$) and Sa_{O_2} ($P < 0.05$). We conclude that Tibetans living at 4,400 m compared with those residing at 3,658 m achieve greater work performance for a given $\dot{V}O_2$ at submaximal and maximal workloads with less cardiorespiratory effort. Am J Phys Anthropol 105:21–31, 1998.

Studies at high altitude have been at the forefront of efforts to understand the interplay of environmental stress, acclimatization, and heredity in human adaptation. Few environments challenge human popula-

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*Correspondence to: Linda S. Curran, Department of Anthropology, Campus Box 103, PO Box 173364, University of Colorado at Denver, Denver CO 80217-3364.

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tions more than high altitude, where cultural practices cannot change the low oxygen pressures (hypoxia) which accompany high altitude residence. Hypoxia limits the ability to transport oxygen, which may limit the ability to perform work, a critical factor in a population's ability to thrive at high altitude.

The performance of exercise or work is a measure of the integrated functioning of the O_2 transport system, with maximal O_2 uptake, $\dot{V}O_{2max}$, a convenient index of that function. In newcomers, maximal O_2 uptake decreases proportionately with ascent to high altitude (Cerretelli, 1980). Most newcomers to high altitude successfully acclimatize within days to weeks of arrival, but even decades of high altitude residence do not restore sea level $\dot{V}O_{2max}$ values. A sojourner arriving in the Tibetan capital of Lhasa (3,658 m) from sea level can expect to reach a $\dot{V}O_{2max}$ that is approximately 70% of his or her $\dot{V}O_{2max}$ at sea level, a value which may increase to as much as 80% of sea level norms after a few weeks of acclimatization (Moore et al., 1994). Should the traveler reside at 3,600 m for years, as the immigrant Han Chinese have done in Tibet, there may be a further small increase to nearly 85% of the initial sea level value (Moore et al., 1994). However, after generations of residence at high altitude, Tibetans residing at 3,658 m have a mean $\dot{V}O_{2max}$ that is 92% of sea level values for sedentary populations (Moore, 1985).

In general, Tibetans seem to be adapted to hypoxia in ways that are not apparent in other native high altitude populations, the latter including historically recent migrants to high altitude (<500 years), such as the Han Chinese (Moore, 1994, 1985; Pei et al., 1989; Sun et al., 1988; Xie and Pei, 1981), as well as those with long population histories (up to 12,000 years) of high altitude residence (Beall, 1982; Moore, 1990; Moore et al., 1992; Winslow et al., 1990). These Tibetan differences include features of the oxygen transport system (Droma et al., 1991; Groves et al., 1993; Sun et al., 1988; Zhuang et al., 1995), maternal-fetal outcomes (Moore, 1990; Niermeyer et al., 1995; Zamudio et al., 1993), and exercise capacity (Curran-Everett et al., 1992a,b; Moore et al., 1992; Ri-Li et al., 1994; Sun et al., 1990). It is certain that Tibetans' ventilatory and hematological characteristics differ significantly from those of Andeans (Beall, 1990; Groves et al., 1993; Zhuang et al., 1993), who have lived at high altitude for approximately half as long as Himalayan populations (Zhimin et al., 1982).

It has been suggested that Tibetans' differences are genetic in basis: that they are better adapted than shorter-resident groups as a result of natural selection for superior abilities to transport oxygen rather than simply by virtue of having been born and raised at high altitude. Yet we have limited knowledge of how their oxygen transport system functions over the full range of environmental exposure to hypoxia. At least one group of investigators has suggested that the altitude of Lhasa (3,658 m) is only moderate, and "experience suggests that chronic mountain sickness is more prevalent in the Tibetan population at higher altitudes, implying that the genetic protection is only partial" (Pei et al., 1989:572). If we are to fully understand Tibetan adaptation to hypoxia, it is important to differentiate between likely genetic vs. acquired physiological contributions to the Tibetan phenotype.

A previous study (Sun et al., 1990) has shown that Tibetan residents of 3,658 m achieve higher maximum workloads, maximum ventilation, and $\dot{V}O_{2max}$ when compared with acclimatized immigrant Han (Chinese) residents of 3,658 m (mean residence duration 8 ± 1 years). Studies have also shown that Tibetan residents of 3,658 m maintain a higher Sa_{O_2} for a given $\dot{V}O_2$ during exercise (Sun et al., 1990; Zhuang et al., 1996). However, many Tibetans reside at altitudes higher than 3,658 m. Furthermore, since Tibetans residing ≥4,000 m seem to have higher activity levels than 3,658 m Tibetans, their lifestyle is a better test of Tibetan adaptability. We decided to compare Tibetans born, raised, and living ≥4,000 m with Tibetans who were born and had resided lifelong in Lhasa at 3,658 m. We reasoned that 4,400 m Tibetans, routinely engaged in the strenuous tasks related to herding animals over mountainous terrain, might have $\dot{V}O_{2max}$ greater than that of more sedentary Lhasa Tibetans at 3,658 m. Such

a finding would support the efficacy of training in the development of higher aerobic capacity in the 4,400 m group, even at higher altitudes with greater hypoxia. Alternatively, were we to find lower or equal $\dot{V}O_{2max}$ in Tibetans residing at 4,400 m, this could implicate limitations imposed by more severe hypoxia on developing higher $\dot{V}O_{2max}$, despite the opportunity for developmental acclimatization or the presence of inherited traits which might advantageously influence oxygen transport in Tibetans.

MATERIALS AND METHODS

Subjects

The participants in our study were 20 Tibetan male residents of ≥4,400 m in the region of Yampa Ching and 16 Tibetan male residents of 3,658 m from Lhasa, Tibet Autonomous Region, China. Subjects granted informed consent to study procedures that had been approved by the Human Research Committees of the University of Colorado Health Sciences Center and the Tibet Institute of Medical Sciences. All were 20–30 years old without known low altitude progenitors and judged healthy by history, physical examination, resting electrocardiogram, and 1 s forced expiratory volume to vital capacity ratio. The residents of ≥4,400 m had been born and raised ≥4,400 m, where they worked as nomadic herders with occasional employment as seasonal laborers (1–3 months per year) in Yampa Ching (approximately 3 h drive northwest of Lhasa). The 3,658 m Tibetans were born and raised in Lhasa and were students or hospital or clerical workers. The 4,400 m Tibetans appeared to be more active than the 3,658 m Tibetans, whose only exercise was routinely riding bicycles at a slow to moderate pace for transportation. In contrast, 12 of the 20 nomadic herders had worked as seasonal laborers seven or more winters; the remaining eight men had worked as seasonal laborers four or fewer winters. The rugged terrain and growing season ≥4,000 m are generally incompatible with agriculture; herding the sure-footed yak provides the means for survival there. Tibetan herders move their animals lower to winter pastures at the same time that they bring the products of their herds to trade in villages located near 4,000 m, the highest altitude where agriculture is still practicable. Their winter employment there as laborers often entails long days and 6 day work weeks, breaking and lifting rock for construction.

Equipment and study techniques

All subjects were studied in Lhasa (elevation 3,658 m, mean barometric pressure 491 torr) within 3 days of descent from 4,400 m and within 2–4 h of their previous meal.

Chest circumference was measured at the junction of the fourth rib with the sternum with the subject at functional residual volume (Weiner and Lourie, 1981). Forced vital capacity was measured in standing subjects using a recording spirometer (8 or 13 L; Warren Collins, Braintree, MA). Measurements were made in triplicate with the highest value accepted.

Resting ventilation and O_2 uptake were measured in subjects who had been sitting quietly for 20 min before study. Subjects breathed through a bidirectional respiratory valve (model 1400; Rudolph, Kansas City, MO) from which O_2 and CO_2 partial pressures were sampled continuously by a fuel cell O_2 analyzer (model 101; Applied Technical Products, Denver, CO) and an infrared CO_2 analyzer (model LB-2; Sensormedics, Anaheim, CA). While the subjects were breathing room air, end-tidal gases and O_2 saturation were monitored for 5 min or until stable values were obtained. Volume was measured by dry gas flowmeter (model RAM 9200; Rayfield, Waitsfield, VT).

Expired gases during rest and exercise were collected in a meterologic balloon, with O_2 consumption and CO_2 production determined by electronic sampling of mixed expired O_2 and CO_2 fractions and measurement of gas volume with correction for volume lost by gas sampling. The gas analyzers were calibrated using gases whose O_2 and CO_2 concentrations had been analyzed on site using the Scholander technique. Arterial O_2 saturation was monitored by an ear oximeter (model 47201A; Hewlett-Packard, Waltham, MA). A four-channel Prime Line (San Francisco, CA) recorder (model R304) was used to record electrical signals from the gas analyzers, ear oximeter, and dry gas meter. Heart rate was measured by electrocardio-

gram (model 500; Sanborn, Waltham, MA). Hemoglobin was measured in resting subjects in duplicate from blood samples obtained by fingerstick without squeezing, using a HemoCue photometer (Atkiebolaget Leo, Helsingburg, Sweden) that had been calibrated previously on site with samples analyzed spectrophotometrically using the cyanomethemoglobin technique.

Exercise was performed on a bicycle ergometer (model 868; Monark, Stockholm, Sweden) at 60 rpm in time to an audible metronome. Pedal revolutions, counted electronically, and the pedal resistance setting, in kiloponds, were used to calculate exercise workload in watts (Astrand and Rodahl, 1977). While the subjects breathed through a low resistance valve (Koegel, San Antonio, TX), samples of mixed expired air were collected in a 200 L meteorological balloon for subsequent measurement of fractional O_2 and CO_2 concentration using the gas analyzers described above. The analyzers were calibrated prior to each measurement of the expired air using ambient air and gas mixtures analyzed on site by the micro-Scholander technique. Mixed expiratory volume was measured using a Parkinson-Cowan ventilation meter previously calibrated against a Tissot spirometer after adjusting for the gas volume lost by O_2 and CO_2 sampling. Electrical signals from the ventilation meter, ear oximeter, O_2 and CO_2 analyzers were recorded on the four-channel recorder. The electrocardiogram was obtained at rest and during each 30 s of exercise (model 500 Viso-Cardiette; Sanborn, Waltham, MA).

The subject began by cycling at 30 watts for 5 min with ventilation and O_2 uptake measured during the last 2 min of exercise. After resting for 5 min, the subject cycled for 2.5 min at ~90 watts, with ventilation and O_2 uptake ventilation measured during the final minute. After another 5 min rest, the subject resumed cycling for 2 min at ~150 watts. This 5 min rest/2 min exercise sequence was repeated thereafter in 30 watt increments, at 180 watts, 210 watts, etc., until the subject showed signs of tiring, at which point the workload increment was halved to 15 watts (e.g., 195 watts if the subject appeared tired at 180 watts). Expired gas collections were made during the final 30 s of cycling at higher workloads. Maximal oxygen uptake, $\dot{V}O_{2max}$, was calculated using standard physiological equations.

Statistics

Values are reported as the mean ± one standard error of the mean (SEM) in the text, tables, and figures. Relationship among variables were identified using a general linear model least squares procedure (SAS, Cary, NC). The 3,658 m and 4,400 m Tibetan samples were compared using one-way, unbalanced analysis of variance with pairwise comparisons of means. Comparisons are considered significant when $P < 0.05$ and reported as trends when $0.05 < P < 0.10$.

RESULTS

By study design, the two groups of Tibetans were similar in height, weight, and age. The 4,400 m compared with 3,658 m Tibetans had greater smoking frequencies and lower forced vital capacities, but there was no difference in chest circumference (Table 1). The 4,400 m Tibetans had lower resting heart rates than 3,658 m Tibetans but similar blood pressure values (Table 1). The levels of resting O_2 consumption and O_2 consumption per unit body weight were lower in the 4,400 m Tibetans (Table 1). However, resting CO_2 production was similar in the two groups, resulting in comparatively higher resting respiratory quotients in the 4,400 m Tibetans (Table 1).

While breathing room air at rest, the two Tibetan samples had similar minute ventilation ($\dot{V}E$) and end-tidal P_{CO_2} (Table 1). The 4,400 m Tibetans had greater ventilation per unit O_2 consumption, higher respiratory frequencies, and higher end-tidal P_{O_2} than the 3,658 m Tibetans, but resting arterial saturation levels (Sa_{O_2}) were similar for the two groups (Table 1).

Maximal oxygen consumption was similar in the two groups (Table 2), but the 4,400 m group reached higher maximal exercise workloads at a lower heart rate (Fig. 1) and $\dot{V}E$ (Fig. 2) with similar arterial O_2 saturation but a higher respiratory quotient (Table 2). A trend toward lower resting hemoglobin levels ($P = 0.087$) (Table 1) resulted in lower calculated oxygen content at maximal effort

TABLE 1. Group characteristics at rest[1]

	3,658 m Tibetans (N = 16)	*P*	4,400 m Tibetans (N = 20)
Height, cm	166 ± 1	NS	166 ± 1
Weight, kg	56 ± 1	NS	57 ± 1
Age, years	24 ± 1	NS	25 ± 1
Hemoglobin, g/dl	18.1 ± 0.3	NS*	17.3 ± 0.3
Chest circumference, cm	85.0 ± 0.7	NS	85.5 ± 0.6
Vital capacity, ml	5,080 ± 127	<.01	4,564 ± 114
Smoking history, pack · year	0.8 ± 0.3	<.01	4.5 ± 0.7
Blood pressure, mmHg, dias/sys	113 ± 2/71 ± 3	NS	117 ± 2/70 ± 2
Resting heart rate, beats/min	72 ± 3	<.01	56 ± 3
$\dot{V}O_2$, ml/min STPD	285 ± 15	<.05	238 ± 13
$\dot{V}O_2$, ml · min^{-1} · kg^{-1} STPD	5.0 ± 0.3	<.05	4.2 ± 0.2
$\dot{V}CO_2$, ml/min STPD	231 ± 18	NS	259 ± 15
$\dot{V}CO_2$, ml · min^{-1} · kg^{-1} STPD	4.1 ± 0.3	NS	4.6 ± 0.3
$P_{ET_{O_2}}$ torr	66 ± 0	<.01	69 ± 1
$P_{ET_{CO_2}}$ torr	31 ± 1	NS	33 ± 1
$\dot{V}_E/\dot{V}O_2$, 1 BTPS · min^{-1} · liters^{-1} STPD	40.6 ± 3.2	<.01	52.8 ± 2.6
Respiratory quotient	0.81 ± 0.04	<.01	1.08 ± 0.04
$\dot{V}_E$, l/min BTPS	11.0 ± 0.9	NS	12.5 ± 0.8
f, breaths/min	17.3 ± 1.1	<.05	20.7 ± 1.0
Sa_{O_2}, on mouthpiece	90.0 ± 0.5	NS	88.7 ± 0.5

[1] Values are means ± SEM; N, number of subjects. $\dot{V}O_2$, O_2 consumption; $\dot{V}CO_2$, CO_2 production; $\dot{V}_E$, minute ventilation; $P_{ET_{O_2}}$, end-tidal P_{O_2}; $P_{ET_{CO_2}}$, end-tidal P_{CO_2}; f, respiratory frequency; Sa_{O_2}, arterial O_2 saturation.
* $0.05 < P < 0.10$.

TABLE 2. Group characteristics during maximal exercise[1]

	3,658 m Tibetans (N = 16)	*P*	4,400 m Tibetans (N = 20)
Maximal heart rate, beats/min	191 ± 2	<.01	176 ± 2
$\dot{V}O_2$, ml/min STPD	2.89 ± 0.04	NS	2.74 ± 0.07
$\dot{V}O_2$, ml · min^{-1} · kg^{-1} STPD	51.2 ± 1.4	NS	48.5 ± 0.2
$\dot{V}CO_2$, ml/min STPD	2.94 ± 0.09	<.01	3.30 ± 0.08
$\dot{V}CO_2$, ml · min^{-1} · kg^{-1} STPD	51.5 ± 1.7	<.01	58.4 ± 1.5
Respiratory quotient	1.01 ± 0.01	<.01	1.20 ± 0.01
$\dot{V}_E$, l/min BTPS	149 ± 6	<.01	127 ± 5
Workload, watts	177 ± 7	<.01	211 ± 6
Sa_{O_2}	83.7 ± 1.2	NS	81.9 ± 1.0

[1] Values are means ± SEM; N, number of subjects. $\dot{V}O_2$, O_2 consumption; $\dot{V}CO_2$, CO_2 production; $\dot{V}_E$, minute ventilation; Sa_{O_2}, arterial O_2 saturation.

in the 4,400 m group (19.3 ± 0.4 compared to 20.6 ± 0.4 ml/dL for the 3,658 m Tibetans, $P < 0.05$). Eleven of the 20 men in the 4,400 m group demonstrated the customary plateau in $\dot{V}O_2$ during the final two workloads, and there were no significant differences in maximum workload or heart rate attained or respiratory quotient at $\dot{V}O_{2max}$ between the 11 who attained a discernable plateau in $\dot{V}O_2$ and the remaining nine who did not (data not shown). It was therefore assumed that $\dot{V}O_{2max}$ was measured at the final workload in all subjects. The attainment of true $\dot{V}O_{2max}$ in the 4,400 m Tibetans is supported by a respiratory quotient of 1.20 at the final workload, despite a lower maximal heart rate when compared with 3,658 m Tibetans (Table 2).

At submaximal workloads, the 4,400 m compared with 3,658 m Tibetans had lower $\dot{V}O_2$ ($P < 0.01$) (Fig. 3), lower $\dot{V}_E$ ($P < 0.01$) (Fig. 2), lower heart rates ($P < 0.01$) (Fig. 1), and lower Sa_{O_2} levels ($P < 0.05$) (Fig. 4).

DISCUSSION

This study examined the relationship between altitude of origin and maximal oxygen consumption ($\dot{V}O_{2max}$, ml/kg − min) among Tibetans who were born, raised, and resident lifelong at 3,658 vs. ≥4,400 m. Maximal oxygen consumption is an integrated measure of the oxygen transport system which can be increased by exposure to higher activity levels and which also has a genetic component (Astrand and Rodahl, 1977). We hypothesized that Tibetans residing ≥4,400 m might show $\dot{V}O_{2max}$ values equal to or greater than values previously obtained in Tibetans residing at 3,658 m. Such a finding would be evidence of a cardiorespiratory reserve capacity in 3,658 m Tibetans that can be activated by exposure to the higher activity levels of the 4,400 m residents, even under the more severe hypoxic conditions

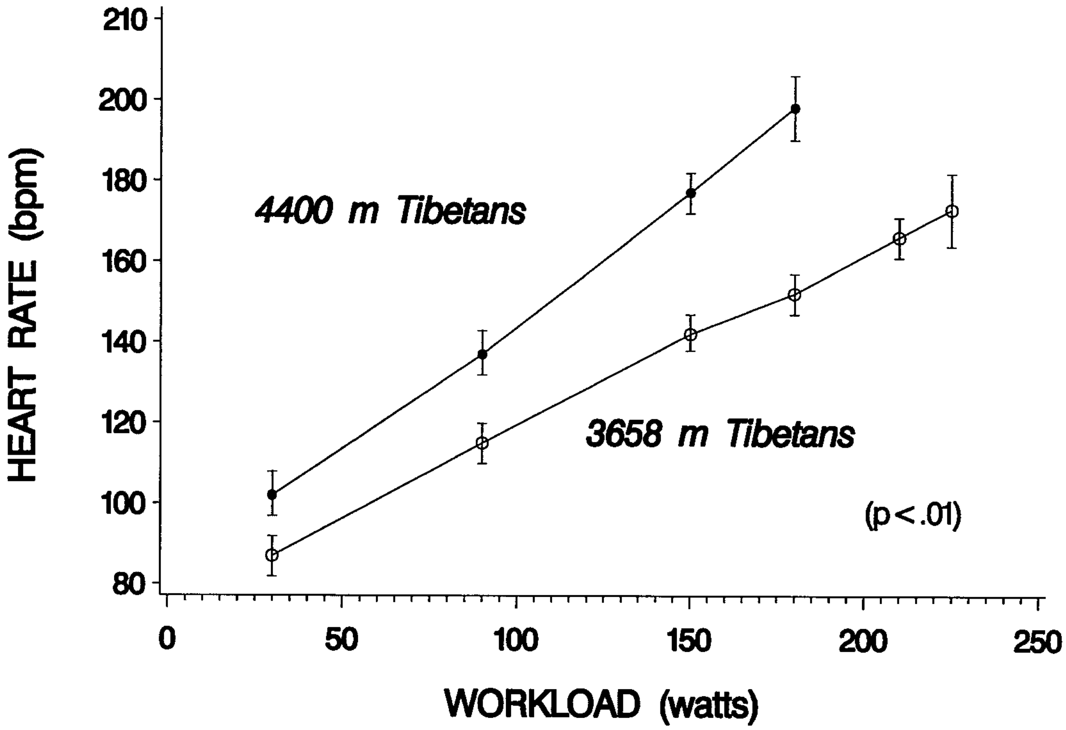

Fig. 1. Heart rates during exercise are lower at submaximal and maximal workloads in 4,400 m compared with 3,658 m Tibetans.

prevalent at 4,400 m. Conversely, a finding of lower $\dot{V}O_{2max}$ in Tibetans residing ≥4,400 m might indicate hypoxia-induced limitation of exercise performance.

We compared 20 Tibetan males born, raised, and working as herders/laborers above 4,400 m with 16 Tibetan men born, raised, and engaged in sedentary occupations in Lhasa. The two groups had similar age, weight, height, and chest circumference (all P = NS) and were tested using the same equipment, measurement protocols, and team of investigators. For the 4,400 m group, exercise testing was performed in Lhasa within 3 days of descent to minimize the possibility of deacclimatization. While more of the 4,400 m sample (16/20 men) than 3,658 m Tibetans (6/16) smoked, there were no significant differences between smokers and nonsmokers residing at 4,400 m in hemoglobin, arterial O_2 saturation, 1 s forced expiratory volume to vital capacity ratio, resting ventilation, end-tidal gases, or levels of resting O_2 and CO_2 consumption. We therefore concluded that smoking did not significantly influence exercise performance in this group.

We found no difference in $\dot{V}O_{2max}$ attained by 4,400 m compared with 3,658 m Tibetans (Table 2). The remarkable finding of this study was that the higher altitude Tibetan group performed more work (reached higher workloads) at the same $\dot{V}O_2$ with less cardiorespiratory effort (i.e., at lower heart rates and lower ventilation levels) when compared with 3,658 m Tibetans (Figs. 1–3). At the same time, the 4,400 m Tibetans experienced a greater arterial desaturation at submaximal workloads than did 3,658 m Tibetans (Fig. 4) and showed lower calculated arterial oxygen contents at all but the highest workloads (≥180 watts). Overall, arterial oxygen content during exercise was lower in 4,400 m than 3,658 m Tibetans (19.83 ± 0.16 vs. 21.15 ± 0.23 ml/dL, $P < 0.01$).

Desaturation with increasing workload among high altitude residents has been noted

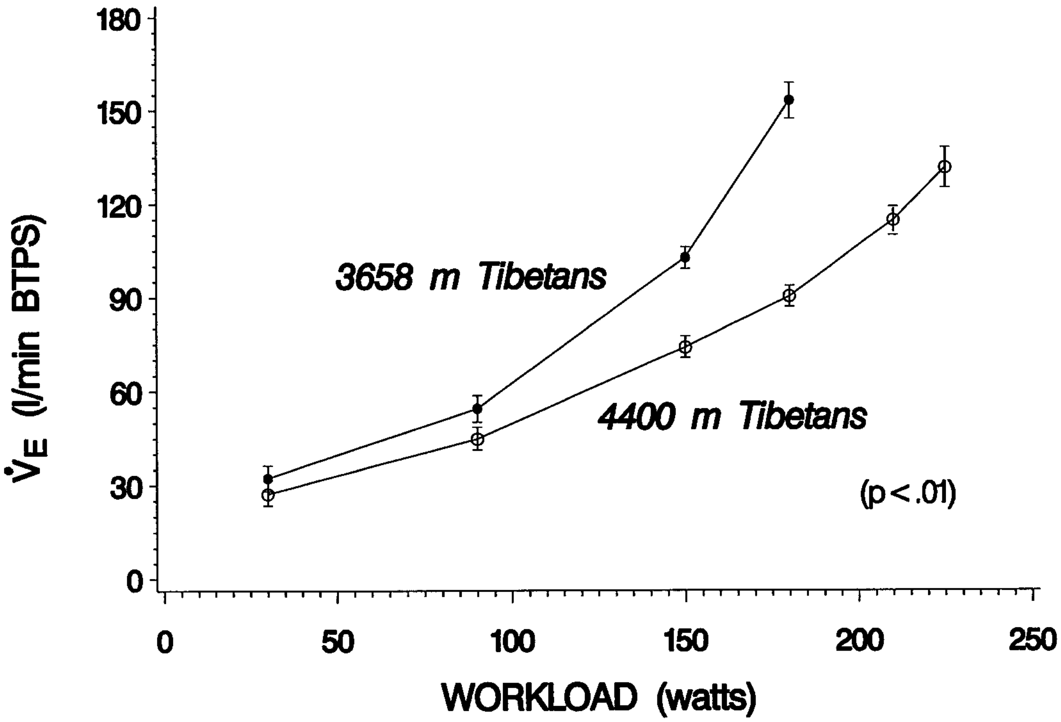

Fig. 2. Ventilation during exercise is lower in 4,400 m than 3,658 m Tibetans.

in previous studies. However, all except three of these studies (Cerretelli, 1976; Houston and Riley, 1947; Zhuang et al., 1996) were conducted with acclimatized nonnative high altitude subjects (Reeves et al., 1987; Schoene et al., 1984; West et al., 1983) rather than lifelong residents exposed to chronic hypoxia. One of these studies found that hypoxic ventilatory responsiveness (HVR) correlates inversely with the drop in Sa_{O_2} from rest to maximum exercise (Schoene et al., 1984); that is, a higher HVR is associated with lesser desaturation during exercise. This is also consistent with data we have reported previously (Curran et al., 1995) for these 4,400 m Tibetan residents: 4,400 m compared with 3,658 m Tibetans have lower HVRs.

It is well known that arterial desaturation can result from diffusion limitation of O_2 transfer during exercise at high altitude (West et al., 1983; Wagner et al., 1987). During exercise, the shortened transit time of blood in alveolar capillaries due to increased cardiac output and a ventilation-perfusion mismatch can diminish the diffusion of O_2 across the alveolar wall into the red blood cells, resulting in lower measured end-tidal P_{O_2} (Dempsey et al, 1975, 1984). Increased alveolar-arterial oxygen gradients would support this possibility, but a previous study instead indicates decreased alveolar-arterial oxygen gradients in 3,658 m Tibetans compared with acclimatized Han residents of 3,658 m (Zhuang et al., 1996). Whether these reduced gradients also exist in 4,400 m Tibetans is unknown. Presumably the lower Sa_{O_2} and trend toward decreased hemoglobin are implicated in the 4,400 m Tibetans' lower arterial oxygen content during submaximal exercise. Although arterial oxygen saturation in 4,400 m Tibetans increases at maximal effort, the increase is insufficient to result in similar calculated arterial oxygen content in the two groups of Tibetans.

Their lower heart rates may indicate larger stroke volumes in 4,400 m Tibetans, since it is clear from a previous study that cardiac output can be maintained in the face of

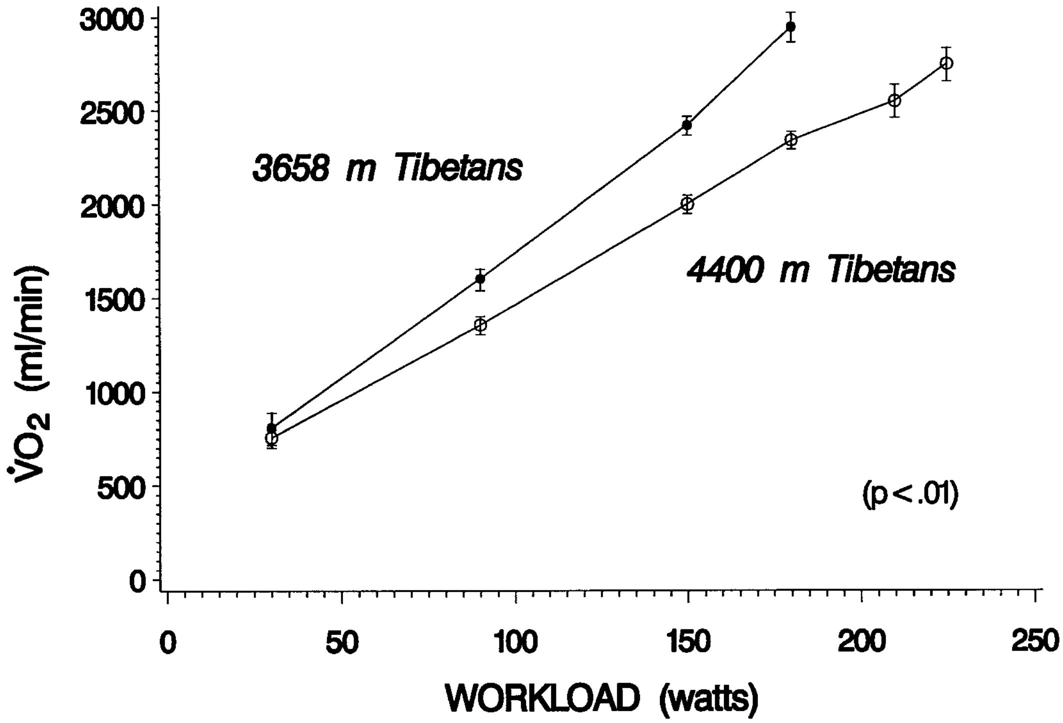

Fig. 3. Tibetan residents of 4,400 m compared with 3,658 m Tibetans have similar $\dot{V}O_{2max}$ and achieve a higher work output at a given $\dot{V}O_2$.

impaired arterial oxygenation (Grover et al., 1976). However, even with larger stroke volumes, the lower heart rates and ventilation levels of 4,400 m compared with 3,658 m Tibetans may limit maximal oxygen uptake. Consistent with this, Tibetans residing at even higher altitude (4,700 m) have been found to have lower $\dot{V}O_{2max}$ (1.85 $\pm$ 0.08 ml STPD/min) than acclimatized Han residents of 4,700 m (Ri-Li et al., 1994) or the 4,400 m Tibetans of our study. The 4,700 m Tibetans also reached higher maximal workloads (168 $\pm$ 4 watts) than acclimatized Han residents of 4,700 m (Ri-Li et al., 1994).

Attaining a higher workload at maximal oxygen consumption could indicate a greater anaerobic capacity in the 4,400 m Tibetans. Lactate was not measured during this or the previous study, so we have no direct way to address this possibility, although another study has found lower lactate values and a higher anaerobic threshold during exercise in Tibetan than in Han residents of 4,700 m (Ri-Li et al., 1994). The 4400 m Tibetans' lower heart rates and ventilation levels across the range of submaximal workloads is inconsistent with a greater reliance on anaerobic than aerobic metabolism generally. A plot of their ventilation as a function of workload appears curvilinear (Fig. 2), as would be expected upon reaching anaerobic threshold, but similar plots of their respiratory quotients and CO_2 production as a function of workload are linear (data not shown). The role of possible training effects in the development of anaerobic capacity was also investigated: a comparison of 4,400 m Tibetans having longer work histories as seasonal laborers ($\geq$7 winters, N = 12) with those having shorter work histories ($\leq$4 winters, N = 8) revealed no differences in $\dot{V}O_{2max}$ or work efficiency (P = NS).

Respiratory quotients at rest in the 4,400 m Tibetan group were surprisingly high (Table 1). The 4,400 m Tibetans also had higher ventilatory equivalents, indicating an increased alveolar ventilation per unit metabolic rate, and higher respiratory fre-

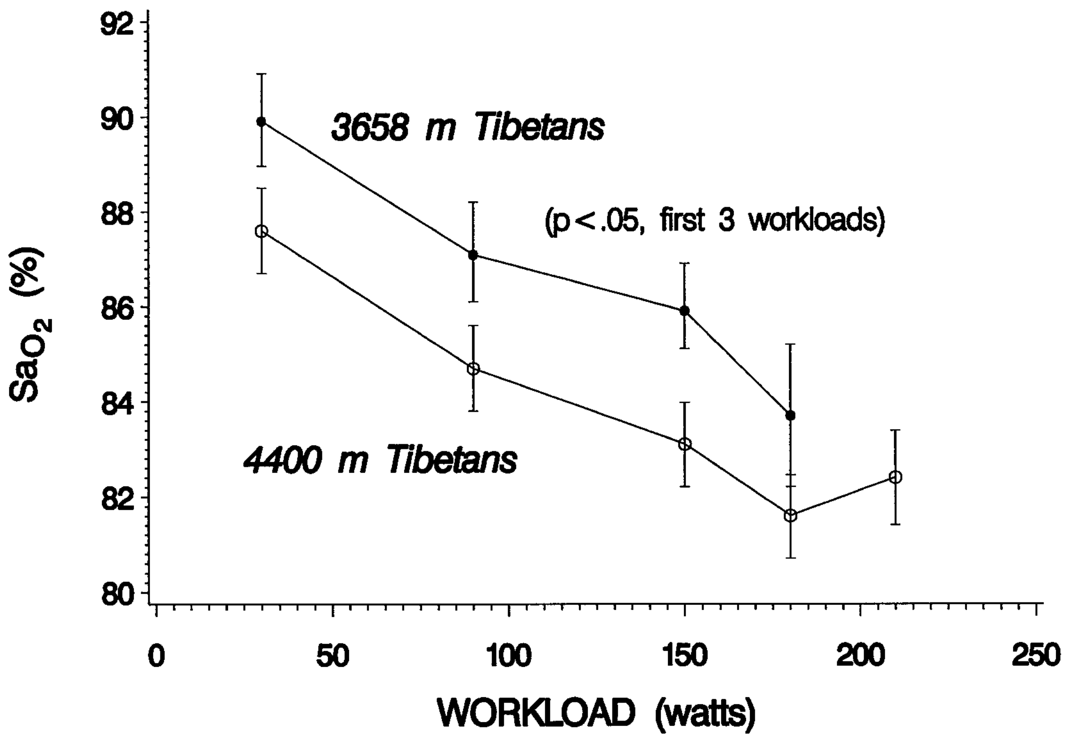

Fig. 4. Tibetan residents of 4,400 m compared with 3,658 m Tibetans had lower Sa_{O_2} at submaximal workloads and similar Sa_{O_2} at maximal workloads during exercise.

quencies (Table 1). However, the high respiratory quotients are not likely to be due to hyperventilation in light of the absence of differences in resting heart rates or end-tidal P_{CO_2} levels in comparison with the 3,658 m sample (Table 1) and the absence of differences in arterial O_2 saturation on and off the mouthpiece in either group, as reported previously (Curran et al., 1995). Further, the level of resting room air ventilation in the 4,400 m Tibetans was consistent with that predicted from their hypoxic ventilatory response curves (Curran et al., 1995). Alternatively, the high respiratory quotients observed might have been a consequence of a high carbohydrate diet or greater gluconeogenesis (Edens et al., 1986). Normally, a higher respiratory quotient would result in a higher end-tidal P_{CO_2} at a given P_{O_2} (Lahiri, 1984), yet we find no evidence of this in the 4,400 m Tibetans. The 4,400 m Tibetans' elevated respiratory quotients may have resulted from their lower O_2 consumption relative to CO_2 production in comparison with the 3,658 m Tibetans, but the lack of a corresponding decrease in resting ventilation remains unexplained. To the extent that a high respiratory quotient at rest indicates relative alkalosis, the loading of O_2 in pulmonary capillaries is enhanced and may ultimately result in a higher tissue P_{O_2} (Bencowitz et al., 1982).

The higher respiratory quotients in 4,400 m compared with 3,658 m Tibetans during exercise require a different explanation. While end-tidal P_{CO_2} gives an acceptable estimate of arterial P_{CO_2} at rest, the possibility has been raised that a true steady state cannot be achieved in exercise studies at altitude (Balke, 1964; Winslow, 1988). Otherwise, there is no obvious explanation for the differences in respiratory quotients during exercise between the two groups of Tibetans.

In conclusion, the lack of increased maximal oxygen uptake with higher activity levels in 4,400 m compared with 3,658 m Tibetans may indicate a hypoxia-induced limitation on the development of aerobic

capacity at the higher altitude. Tibetans residing at 4,400 m do not have larger vital capacities relative to 3,658 m residents, nor do they raise arterial O_2 saturation by greater exercise ventilation, as do 3,658 m Tibetans (Zhuang et al., 1993). Greater stroke volume in 4,400 m compared with 3,658 m Tibetans remains a possibility, but our findings do not appear consistent with 4,400 m Tibetans having relatively greater tissue O_2 extraction. Nevertheless, in spite of lower ventilation and greater oxygen desaturation during exercise, it is clear that the 4,400 m Tibetans did not suffer impaired exercise capacity. Nor did the 4,400 m Tibetans' lower heart rates and ventilation levels across the range of submaximal workloads support a greater reliance on anaerobic than aerobic metabolism generally. Greater work performance at the same $\dot{V}O_2$ across a range of submaximal workloads implies increased energy production from a given oxygen uptake (i.e., increased work efficiency). This has been variously hypothesized to involve a tighter coupling of ATP demand to ATP supply (Matheson et al., 1991) and/or greater efficiency of chemical to mechanical energy coupling (Hochachka 1989; Hochachka et al., 1991). However, the mechanism for this increased efficiency, also noted in a previous study of Tibetans residing at 4,700 m (Ri-Li et al., 1994), has yet to be identified.

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